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- Group III: Claims 60-62, drawn to compositions, corresponding new claim 111;
Group IV: Claims 57-58, drawn to a method to reduce immunogenicity;
Group V: Claim 59, drawn to a method to prepare an interferon conjugate, corresponding new claim 108; and
Group VI: Claims 63-65, drawn to methods to treat a mammal, corresponding new claims 112-115.

Applicants respectfully submit that a search of group Group III would be co-extensive with the search of Group I and would represent no undue burden. As such, Applicants respectfully request rejoinder of inventions Groups I and III. Applicants elect for prosecution Group I, as represented by newly-added claims 73-95, and, claim 111 should rejoinder of Groups I and III be effected.

B. The invention was further restricted as follows:

"Inventions 1-38 as they pertain to SEQ ID NO:1-SEQ ID NO:38, respectively." See, *Office Action, page 4, item 7.*

Applicants respectfully traverse the requirement to restrict the invention between 38 individual sequences provided in the specification. Applicants respectfully request the Examiner to reconsider and withdraw the requirement to restrict the invention by the SEQ ID NOs listed in the application in view of the reasons discussed in more detail below, most particularly because the restriction requirement as written makes it impossible for the Applicants to pursue claims to their invention.

In an effort to be fully responsive to this Office Action, Applicants elect Group I (plus Group III as noted above), and a species as represented by SEQ ID NOs:28, 33, 34, and 35, which, as will be shown below, together represent a species of interferon β polypeptide variant comprising the substitutions Q49N+Q51T.

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Restriction of the Invention to SEQ ID NOs 1-38 is Inappropriate

In an effort to demonstrate to the Examiner why it is inappropriate, and in fact impossible, to restrict Applicants' invention among SEQ ID NOs:1-38, below is a brief description of these sequences:

SEQ ID NO:1 is the cDNA sequence of wild-type human IFN-beta (GenBank Accession number M28622).

SEQ ID NO:2 is the protein sequence of wild-type human IFN-beta.

SEQ ID NO:3 through SEQ ID NO:20 are oligonucleotide primers which were used to prepare a synthetic, codon-optimized DNA construct encoding IFN-beta (SEQ ID NO:2) as detailed in Example 1. Applicants respectfully point out that it would be meaningless to attempt to restrict the invention according to any one of SEQ ID NOs:1-20, since SEQ ID NOs:1-20 represent, or encode, all or parts of wild-type human IFN-beta, which is not the claimed invention.

The remaining sequences specified by SEQ ID NO: in the application are either mutagenic oligonucleotide primers which were used in at least pairwise fashion to incorporate exemplary mutations into the synthetic, codon-optimized IFN-beta DNA construct described above, or, are primers which were used simply for amplification/subcloning purposes:

SEQ ID NOs:21 & 22 are forward and reverse DNA primers used to incorporate a K45R mutation (as described in Example 2).

SEQ ID NOs:23 & 24 are forward and reverse DNA primers used to incorporate an F111N mutation (as described in Example 2).

SEQ ID NOs:25 & 26 are forward and reverse DNA primers used to incorporate an R113T mutation (as described in Example 2).

SEQ ID NOs:27 & 23 are forward and reverse DNA primers used to incorporate a K19R mutation (as described in Example 2).

SEQ ID NOs:28 & 29 are amplification primers used to amplify & subclone synthetic DNA constructs into other expression vectors (as described in Example 3).

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SEQ ID NOs:30 & 31, and SEQ ID NOs:26 & 32, are two overlapping primer sets used to construct F111N plus R113T (as described in Example 5).

SEQ ID NOs:28 & 33, and SEQ ID NOs: 34 & 35, are two overlapping primer sets used to construct Q49N plus Q51T (as described in Example 6).

SEQ ID NOs:36 & 33, and SEQ ID NOs: 34 & 35, are two overlapping primer sets used to construct Q49N, Q51T, F111N, R113T (as described in Example 7).

SEQ ID NOs:37 & 26 are forward and reverse DNA primers used to construct S(-1)A plus M1Q (as described in Example 15).

SEQ ID NOs:38 & 26 are forward and reverse DNA primers used to construct S(-1)AQ (as described in Example 15).

As the Examiner can see, pairs (and, in some instances, pairs of pairs) of primers were used to prepare exemplified mutations. In some instances, an individual primer (such as, SEQ ID NO:26, or SEQ ID NO:33) was employed in several different mutagenesis reactions. Thus, restricting the invention by individual primer sequences is simply meaningless, and would render it impossible for Applicants to capture the intended scope of their invention.

Proposed Species Election

In an effort to expedite prosecution, Applicants have cancelled claims 1-72 without prejudice to subsequent renewal, and have introduced herein new claims 73-115. Applicants elect claims 73-95 drawn to Group I (polypeptides), and claim 111 should rejoiner between Group I and III be effected.

Applicants further respectfully request that, instead of further restricting the invention by SEQ ID NO (which is tantamount to imposing a restriction requirement on an individual claim), the Office instead examines a "reasonable number" of species encompassed by the claim. See, 37 C.F.R. §1.146 and MPEP §809. A species election, pursuant to MPEP §803.02, strikes an appropriate balance between the concerns of the Office regarding administrative matters and unduly burdensome examination, and the rights of an inventor to claim an invention as it is

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contemplated, provided the dictates of 35 U.S.C. §112 are complied with. See, the MPEP at 803.02. See also, *In Re Wolfrum* 179 USPQ 620 (C.C.P.A. 1973) and *In re Kuehl* 177 U.S.P.Q. 250 (C.C.P.A. 1973). Unlike a restriction requirement, a species election does not preclude Applicants from pursuing the original form of a claim in subsequent prosecution, nor does it force Applicants to file multiple divisional applications which are incapable of capturing the intended scope of the their invention.

Applicants therefore propose to elect for initial examination the species of interferon β polypeptide variant comprising the substitutions Q49N + Q51T. All claims pending with entry of this amendment read on the proposed elected species. In the event the elected species is found to be patentable, Applicants request, pursuant to the procedure outlined in MPEP §803.02, that additional species recited in claim 73 be examined.

CONCLUSION

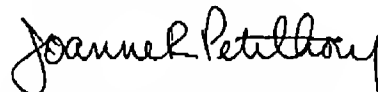
In the event the Examiner intends to maintain the original restriction, Applicants request an interview with the Examiner and with SPE Gary L. Kunz prior to preparation of any additional written action by the Office.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 298-5452.

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Respectfully submitted,



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